70. (New) The plurality of primer pairs of claim 12, wherein at least one primer pair comprises SEQ ID NOS: 3 and 4.

71. (New) The plurality of primer pairs of claim 70, wherein at least one primer pair comprises SEQ ID NOS:19 and 20.

72. (New) The method of claim 25, wherein the primer pair comprises SEQ ID NO:3 and 4.

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73. (New) The method of claim 72, wherein, upon generating a PKD1-specific amplification product, the method further comprises:

contacting the PKD1-specific amplification product with at least a second primer pair comprising SEQ ID NOS:19 and 20; and

identifying the presence or absence of a mutation in the nested amplification product, thereby detecting the presence or absence of a mutation in the PKD1 polynucleotide in the sample.

74. (New) The method of claim 44, wherein the at least one primer pair comprises SEQ ID NO:3 and 4.

75. (New) The method of claim 53, wherein the second primer pair comprises SEQ ID NOS:19 and 20.

The Reply to Restriction Requirement

Responsive to the Restriction Requirement, Paper No. 10, dated May 23, 2002, Applicant elects with traverse the species, primers SEQ ID NOS: 3 and 4, nested primer pair SEQ ID NOS: 19 and 20, polynucleotides containing PDK1 mutations located in regions amplified by said nested primers, the methods of detecting this specific region with these specific nested primer pairs and kit containing these same primer pairs to amplify said specific region.

It is Applicant's understanding that the elected invention is claimed in Claims 1-66 as well as 68-75, readable on the elected species. Applicant reserves the right to file a continuing application or take such other appropriate action as deemed necessary to protect the non-elected inventions. Applicant does not hereby abandon or waive any rights in the non-elected inventions.

The requirement is being traversed for the reasons set forth in detail below.

The Restriction Requirement

The restriction sets forth 44 different Groups of inventions. Inventions in Groups 1- 43 comprise the subject matter that is defined by the Claims 1-66 as filed as well as Claims 68-75. Group 44 encompasses subject matter defined by the Claim 67. The instant traversal is limited to Groups 1-43 for which recombination is requested.

The Examiner states that Groups 1- 43 include inventions that are patentably distinct in structure and physiochemical properties because they are each drawn to different nucleic acid sequences. The Examiner does not provide the details of which sequences belong to each of the 43 Groups. The Examiner further states that the compositions are utilized in different methodologies, e.g. such as in hybridization to different regions of the same gene, and that no Group requires the invention of the other, since each invention has different primary sequence.

It appears that a further restriction is applied. The Examiner states that "the Applicant must elect a single primer pair from nucleic acid sequence SEQ ID NOS: 3-18, a single nested primer pair that corresponds to the elected primer pair consisting of SEQ ID NOS: 19-50, 51 and 61 and SEQ ID NOS: 62 to 92, 113, and 97 to 112, and a single polynucleotide region containing

a mutation as specified in Claim 20 that is detected specifically by the elected primer pair and nested primer pair." (Page 3, last paragraph.) The Applicant is advised that examination will be restricted to only the elected SEQ ID NOs. and that such sequence election requirement should not be construed as species election. The examiner appears to imply that the generic invention will not be examined.

Groups 1- 43 should be rejoined

Under the decision of *In re Weber*, 198 USPQ 328 (CCPA 1978) and *In re Haas*, 198 USPQ 334 (CCPA 1978), it is improper for the Patent Office to refuse to examine that which applicants regard as their invention unless it lacks unity of invention. (MPEP 803.02.) Unity of invention exists where the compounds share a common utility and a substantial structural relationship, disclosed as being essential to that utility.

Nucleic acid sequences of Groups 1- 43 all share a common utility, namely, they comprise primers useful for selectively amplifying a region of PKD1 gene, but not a corresponding region of a PKD1 homolog. Also provided are nested primer pairs useful for performing nested amplification of a PKD1-specific amplification product of a PKD1 gene. Therefore the nested primers also share the common utility of the nucleic acid sequences of Groups 1- 43.

Nucleic acid sequences of Groups 1- 43 all share a structural feature disclosed as being essential to the above specified utility. Specifically, the primers are all polynucleotides with sequences that specifically hybridize to a PKD1 gene. As in *In re Weber* and *In re Haas*, the mere fact that the members of the claimed genus are not identical in chemical structure does not destroy the fact that all members of the genus have a substantial common core structure.

The Examiner states that, since each species of nucleic acid encodes a different polypeptide with distinct biochemical and physical properties, each nucleic acid has acquired a

separate status in the art, and each nucleic acid requires a different search which is not coextensive in scope with other claimed nucleic acids.

Firstly, the Examiner's analysis has become tautological. By definition, chemical species embraced within any given chemical genus must differ in some manner, e.g., by their chemical structure or sequence or, in some instances, the polypeptide they individually encode. Further, it is expected that any two chemicals having some difference in chemical structure are likely to have some difference in properties. Thus, the Examiner's observation that the genus embraces multiple chemical species is always true in each and every generic claim. However, it cannot be true that a restriction is justified by this observation alone. According to the Examiner, because the species differ in some manner, the search is alleged to be not coextensive and thus, there is an undue search burden justifying a restriction requirement. Indeed, the Examiner can define any search of a species to be so narrow as not to be coextensive of another species, irrespective of how closely related the two species may be. In this case, the Examiner did not offer any guidance as to what the search would be or would include and could very well be limited to include only a single species. Using this logic, any genus presented in a claim could be subject to restriction at the discretion of the Examiner. Again, the restriction requirement is so lacking details to make a discussion of the actual search required by the multiple species embraced within the generic claims impossible.

Certainly, such observations, as made by this Examiner, were not accepted in *Weber* and *Haas*, which presented the Office with claims to a genus of multiple species subject to a different search. That is certainly not the test applied in MPEP 803.02 which clearly contemplates the examination of structurally related (not identical) species which do not share a coextensive search. Likewise identity in physical and biochemical properties is not required by this jurisprudence to present claims drawn to multiple embodiments in a single application. Thus, the Examiner's position is clearly not well founded in the law. More is required for the Examiner to

justify a restriction than the observation that a genus claims multiple species and the allegation that the search is not coextensive.

Furthermore, the Examiner's reference to various nucleic acids as encoding different proteins misses the invention scientifically. The invention relates to diagnostic methods of identifying the presence of PKD1 gene sequence in a sample, the products useful in such methods (e.g. primers, primer pairs, nested primer pairs), and kits containing such products. Primers are, in general, too short to encode a protein themselves. Thus the observation that the various primers described in this application will encode different proteins is not technically relevant, even if it were possible.

Any search by the examiner of proteins encoded by primers will not be expected to identify the most relevant art. The most relevant search will likely be of the gene sequence sought to be detected, i.e. that of PKD1 gene.

According to the Opinion of *In re Weber*, 198 USPQ 328 (CCPA 1978), third paragraph:

> As a general proposition, an applicant has a right to have *each* claim examined on the merits. If an applicant submits a number of claims, it may well be that pursuant to a proper restriction requirement, those claims will be dispersed to a number of applications. Such action would not affect the right of the applicant eventually to have each of the claims examined in the form he considers to best define his invention. <u>If, however a single claim is required to be divided up and presented in several applications, that claim would never be considered on its merits.</u>

Claims of the Groups 1 - 43 comprise generic claims drawn to the use of nucleotide sequences that share a common utility and a substantial structural relationship and that define the Applicant's invention. Restricting the species of these generic claims to very specific pair

combinations in multiple applications will ensure that the generic invention will never be considered on its merits.

Furthermore, the sheer number of the Groups of invention set forth by the Examiner all but precludes the Applicant from exercising his rights to having each claim examined on the merits. The precise number of inventions identified is unclear from the structure of the restriction requirement. There may be 44 inventions requiring 44 applications. The failure to provide reasonable direction in the restriction leaves open a possibility that each and every sequence, pair of sequences and nested pairs requires its own application. In this case, the number of applications becomes exceedingly high. In either case an undue burden is placed on the Applicants. The burden of filing 44 or more different applications within a claim is tantamount to a rejection of that claims and a refusal to examine the Applicant's invention.

Applicants therefore request that both restriction requirements be withdrawn and replaced with requirements for election of species (i.e., SEQ ID NOs.). Applicants request further that the elected species be examined, and, upon a finding that the elected species is allowable, that the entire scope of the claims be examined. Applicants hereby elect primers SEQ ID NOs: 3 and 4, nested primer pair SEQ ID NOs: 19 and 20, polynucleotides containing PDK1 mutations located in regions amplified by said nested primers, the methods of detecting this specific region with these specific nested primer pairs and kit containing these same primer pairs to amplify said specific region.

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (858) 677-1456.

Respectfully submitted,

Date: 11/21/02

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